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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,879	04/09/2007	**Augustinus Bader**	50326/006001	8676

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
11/30/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,879	BADER, AUGUSTINUS	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36 and 39-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36 and 39-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

Applicant's arguments, filed 28 September 2010, have been entered in full. Claims 1-35, 37 and 38 are canceled. Claims 36, 39-44 are under examination.

Withdrawn Objections And/Or Rejections

The rejection to claims 36, 39 and 40 under 35 U.S.C. 103(a) as being unpatentable over Buemi et al. (Acta Derm Venereol. 82:411-417, 2002) in view of Kim et al. (Journal of Burn Care & Rehabilitation, 14(5):541-3; Sept-Oct 1993), Brines et al. (US 2003/0104988 A1) and Bhaskaran et al. (United States Patent Application Publication US 2004/0136952 A1), as set forth at pages 5-8 of the previous Office Action (28 June 2010), is *withdrawn* in view of Applicant's argument that Buemi et al. do not teach topical administration of EPO (28 September 2010).

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36 (and dependent claims 39, 40, 43 and 44) remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for healing of burn wounds in an individual using a skin graft, the method comprising **topically applying erythropoietin (EPO) to said wound**,

does not reasonably provide enablement for:

a method for healing of burn wounds in an individual using a skin graft, the method comprising **topically applying erythropoietin (EPO) to said skin graft, then applying said skin graft to said wound**.

The basis for this rejection is set forth at pages 3-5 of the previous Office Action (28 June 2010).

Applicant argues that Maggi is not relevant to the claimed invention. Applicant argues that Maggi teaches that a pre-formulated anti-bacterial cream (Sulfamylon cream) caused desiccation and cytotoxicity in skin grafts. Maggi teaches that the problem identified by the Office was solved with a simple 5% aqueous solution of the same active ingredient, which was sufficient to have an anti-bacterial effect without exhibiting the desiccation and cytotoxicity of the cream formulation. Applicant maintains that the Office has not cited, and nor has the Applicant found, a reference teaching that topically applied EPO would intrinsically cause desiccation and cytotoxicity in skin grafts. Applicant argues that the Office has not provided any rationale for why one skilled in the art would expect an antibacterial topical formulation to have had similar properties to a topical formulation containing a biological ingredient like EPO protein. Applicant argues that Maggi does not stand for the proposition that skin grafts cannot be pre-treated with a topical formulation prior to application to a wound; rather, Maggi teaches that one particular formulation of a drug other than EPO was not compatible with this approach, while other formulations were compatible. Applicant maintains that Maggi is not evidence that the preparation of topical formulations of EPO is a particularly unpredictable field of scientific endeavor.

Applicant's arguments have been fully considered but are not found persuasive. The instant claims encompass topically applying EPO directly to a burn wound on an individual using a skin graft ***AND*** topically applying EPO to a skin graft (in culture, *in vitro*; i.e. not attached to an individual) and then applying said skin graft to a burn wound on an individual. The Examiner's argument is that the specification fails to teach that EPO can be topically applied *in vitro* to cultured skin grafts, which are then transported to an individual. Maggi is relevant to the claimed invention because it teaches that new epithelium is very vulnerable to desiccation or lysis. Skin grafts in culture are avascular so they are very fragile. The reference was cited to demonstrate that tissue which has already been grafted on to an individual is vulnerable to desiccation or lysis *AND* that Maggie only teach the use of the solution which is topically applied ***after*** the skin is grafted onto the subject. A skin graft *in vitro* would be more delicate and susceptible to desiccation. Applicant argues that Maggi does not stand for the proposition that skin grafts cannot be pre-treated with a topical formulation prior to application to a wound. The Examiner maintains that Maggi et al., the submitted art and most importantly the instant specification *all fail* to teach that skin grafts in culture can be topically applied with a formulation prior to application to a wound on an individual. The instant specification fails to teach how the EPO formulation is topically applied. For example, is EPO brushed on the graft in culture? Contrary to Applicant's assertion, the topically applied EPO does not have to have similar properties to an antibacterial topical formulation. Desiccation and lysis can occur to *in vitro* grafts just by physically coating avascular tissue with EPO. The specification fails to teach the amount of time (i.e. time

window) the topically applied EPO stays on the skin graft before it is grafted on the burn patient. For example, is there a minimum amount of time the topically applied EPO must stay on the *in vitro* skin graft before it can be grafted on the burn patient? Is there a maximum amount of time before the *in vitro* skin graft and topically applied EPO are no longer effective? Is the EPO in a gel or a lotion? How would the EPO gel or EPO lotion stick to skin grafts in culture?

Undue experimentation is a conclusion reached by weighing all of the *Wands Factors,* if one skilled in the art can readily anticipate the effect, then there is predictability in the art. In the instant case, the art is unpredictable based on the evidence provided. The evidence for the degree of predictability in the art also relates to the amount of direction needed in the specification. A considerable amount of time is permissible for the quantity of experimentation needed to make or use the invention based on the disclosure. However this depends on if the invention is routine or if the skilled artisan is given sufficient direction or guidance. In the instant case, the experimentation is not routine and the specification has provided no guidance. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 41-43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Buemi et al. (Acta Derm Venereol. 82:411-417, 2002) in view of Dunn, J.M. (Abstract; Clinics in podiatric medicine and surgery, Vol. 4/No. 2, pages 413-418, April, 1987), Brines et al. (US 2003/0104988 A1) and Bhaskaran et al. (United States Patent Application Publication US 2004/0136952 A1). The basis for this rejection is set forth at pages 8-10 of the previous Office Action (28 June 2010).

Applicant argues that Buemi does not teach the topical administration of EPO and consequently does not teach administration of EPO into blood coagulum. Applicant argues that as this limitation is not taught by any of the cited references, this rejection could be withdrawn on this basis alone.

Applicant's arguments have been fully considered but are not found persuasive. Claim 41, as recited, is not limited to or embraces a particular type of administration. The claim does not specify, "topically administering EPO". Claim 41 recites, "..mechanically debriding the wound bed and then introducing EPO into the blood coagulum". Because the instant claim does not state *how* EPO is introduced, it encompasses all types of administration.

Applicant argues that Dunn teaches that vigorous, repeated debridement is essential and is to be followed by high pressure irrigation and frequent wet to dry fine mesh gauze dressings. Applicant cites MPEP 2122.

"The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme

Court in KSR noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that "'[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness"

Applicant argues that the Office fails to provide any rationale for how the method of Dunn is compatible with the claimed method of administering EPO to blood coagulum following debridement. Applicant contends that the brief description of Dunn cited by the Office appears to teach cleaning and repetition of irrigation and drying in order to minimize blood coagulum prior to wound dressing. Applicant argues that neither Buemi nor Dunn teach or suggest the administration of EPO to blood coagulum, and one skilled in the art would not have been motivated to combine the teachings of Dunn with the administration of EPO to the blood coagulum.

Applicant's arguments have been fully considered but are not found persuasive. As was stated above, claim 41 does not recite, "topically administering EPO" and thus encompasses all types of administration. The Examiner takes no issue with Applicant's comments regarding MPEP 2122. The Examiner has articulated the rational to support the legal conclusion of obviousness. Dunn **does not** teach the use of debridement to minimize blood coagulum prior to wound dressing as stated by Applicant. Dunn teaches the use of debridement to remove necrotic/devitalized tissue and old blood. Dunn states that this process helps with effective wound healing and decreases the risk of infection. Further, Dunn states that choice of bandaging material should be determined by the desired action on the wound, such as protection, debridement and so on. Thus Dunn's teachings can be modified accordingly. It would be obvious to properly prepare

the wound base before administering EPO. Blood coagulum is merely clumping of blood. Buemi et al. teach that EPO induced vascularization and increased the number of capillaries and neoangiogenesis in rats (Figure 5 and page 416, 3rd full paragraph). Thus EPO is in the blood system. It would be obvious to use mechanical debridement, as taught by Dunn, to remove dead tissue from a wound before administering EPO to increase the number of capillaries, induce neoangiogenesis and to induce the wound-healing process in both the early and late stages of wound injury as taught by Buemi. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the

statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647
/R. M. D./
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11/23/10